

PATENT

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Application of : Alan R. Hirsch  
Serial No. : 09/211,507  
Filing Date : December 14, 1998  
For : USE OF ODORANTS TO ALTER BLOOD FLOW TO THE  
VAGINA (as amended) #17  
M.G.J  
7/17/01  
Group Art Unit : 3736  
Examiner : C. Tate  
Attorney Docket No.: INS-31061

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**DECLARATION OF ALAN R. HIRSCH, M.D.**

I, Alan R. Hirsch, M.D., F.A.C.P., applicant in the above-identified patent application, declare and say as follows:

1. I am a neurologist and psychiatrist, and have held the position of Neurological Director of the Smell and Taste Treatment and Research Foundation, Chicago, Illinois since 1988. I received a Bachelor of Science (B.S.) degree from the University of Michigan in 1976, and an M.D. from the University of Michigan in 1979. My research has been in the area of identifying the physiological role that odors play in human behavior including weight loss, learning, perception of physical space, exercise endurance, and the treatment of migraine headaches and insomnia, and increasing blood flow to the penis to enhance penile erection. I have been issued six U.S. patents related to the use of odorants: to alleviate headaches, to alter learning capacity, to treat male impotence (increase penile blood flow), to alter perception of relative space of an area, and to assay for somatization disorders and for psychiatric disorders (depression). I have published more than 100 articles on the psychological power of scent, and my studies have been published in the *Journal of the American Medical*

*Association* (JAMA) and other journals. At the Foundation, I test patients with chemosensory, smell, and taste disorders. Diagnostic evaluation typically includes a neurological examination and a variety of smell and taste tests.

2. I make this Declaration in support of the patentability of the claims of the above-identified patent application. The claims of the application are to a method of administering an odorant to a female individual to alter (increase or decrease) blood flow to the vagina. As I understand, the Examiner in an Office Action mailed January 31, 2001 has questioned the believability of the claimed method, and contends that the observed effects are the result of a placebo-effect.
3. The method of the invention was used to administer a series of odorants to female volunteers to test and evaluate the effect of the odors on blood flow to the vagina. The study was a randomized, double-blind test in which neither the female subjects nor the test administrators knew which scents were being tested during the study. The methods used and details of the study are provided in the attached APPENDIX.
  - a) Briefly, each of 30 female test subjects underwent preliminary standardized tests to measure olfactory ability, and were queried as to sexual history, sexual preferences, odors hedonics, and orgasmic functioning. The subjects were then positioned on an examination table and a photoplethysmograph, which measures pulse pressure as an indication of change in blood flow, was placed into the vagina of the subject.
  - b) After a three minute acclimation period, an untreated, non-odorized (control) surgical mask was applied over the subject's nose and mouth for one minute, and blood flow to the vagina was measured. The mask was removed and the subject was asked to identify the odor and whether they liked or disliked it. The subject was then randomly presented with a series of ten masks that were scented with an odorant

or odorant mixture. The ten odorant(s) that were administered are listed in TABLE 1 of the APPENDIX. Changes in pulse strength were recorded on a continual basis. A three minute "washout" period took place between each mask.

- c) At the end of the testing, a second untreated, non-odorized (control) mask was applied. Recordings were obtained, with the two control masks used as markers of a baseline measurement.
4. The effects of the odors were assessed by comparing the reading for each odor to the average reading of the two control masks. The data was statistically analyzed using non-parametric tests: the Signed Rank Test, Wilcoxon Rank Sum Test, and Spearman's Rank Correlation Coefficient. Statistical significance was defined a "p" value less than or equal to 0.05. The effect of each odor on blood flow to the vagina was calculated based on changes from the average of the blood flow measured while wearing the control masks.
5. Each female subject also underwent a series of questionnaires to obtain demographic data, sexual history data including sexual conduct and behavior, olfactory preference, and orgasmic functioning. Each subject also completed Sexual Arousal Ability Inventories, which were standardized tests to access ease of arousability and degree of anxiety induced by various sexual activities.
6. The results are summarized in TABLES I-V.
- a) TABLE I shows the average change of blood flow to the vagina of the entire group of test subjects (n=30) for each of the odorant(s) that were administered.
- b) TABLES II-V show the average change in blood flow to the vagina for different subgroups of female subjects: (II) females highly aroused with masturbation,

(III) females inhibited/minimally aroused with masturbation, (IV) females positively aroused by manual genital stimulation by a partner, and (V) females negatively aroused by manual genital stimulation by a partner.

c) There were also differences found among women according to the frequency of orgasmic episodes (i.e., multi- or mono-orgasmic).

7. The results indicated that certain odors can be administered to a female to increase or decrease blood flow to the vagina.

a) in the overall group of females, a mixture of a licorice-based and cucumber odorants, a baby powder odorant, and a mixture of pumpkin pie and lavender odorants had the greatest effect on increasing blood flow to the vagina (+11% to +13%);

b) in the overall group of females, the cherry odorant, the charcoal barbecue smoke odorant, and the licorice-based odorant had the greatest effects on decreasing blood flow to the vagina (-18% to -12%).

c) The licorice-based odorant and cucumber combination was the most effective odorant overall.

8. The results also indicated that women responded differently depending on their preferences of sexual activities and behaviors.

a) In those female individuals who were positively sexually aroused with masturbation or by manual manipulation of the genitals, a baby powder odorant, a mixture of a licorice-based odorant and banana nut bread odorant, a mixture of a licorice-based odorant and cucumber odorant, a floral-aldehydic perfume fragrance, a mixture of lavender and pumpkin pie odorants, and a mixture of baby powder and

chocolate odorants were particularly effective in increasing blood flow to the vagina (by about 10-30 %).

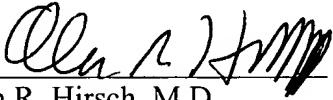
b) In those female individuals who were negatively or minimally sexually aroused with masturbation or by touching or manipulation of the genitals by a partner:

- (i) a licorice-based odorant alone, a mixture of a licorice-based odorant and cucumber odorant, a charcoal barbecue meat odorant, a cherry odorant, a men's cologne (e.g., Old Spice), and a floral-aldehydic perfume fragrance (e.g., Chanel No. 5) were particularly effective in reducing blood flow to the vagina (by about 10-20%); and
- (ii) a baby powder odorant was effective in increasing blood flow to the vagina (by about 16%).

9. I interpret the data of paragraphs 6 through 8 to indicate that the administration of certain odorants or mixtures of odorants to a female individual with a normal olfactory ability can alter the individual's flow to the vagina by about -20% to about +30% compared to baseline blood flow to the vagina (no odorant given). I further interpret the data to indicate that administering certain odorants and mixtures of odorants to a female individual can result in an increase or decrease in blood flow to the vagina of a female individual, which change can be correlated to the individual's preferences of sexual activities and behaviors.
10. I conclude, in view of the foregoing results, that blood flow to the vagina of a female individual can be altered by administering certain odorants and odorant mixtures.

11. I further declare that all statements made herein of my knowledge are true and that all statements made on information and belief are believed to be true, and further, that these statements are made with the knowledge that willful false statements and the like are punishable by fine or imprisonment, or both, under Section 1001 or Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of this application or any patent issuing thereon.

Date: 6/28/01

By:   
Alan R. Hirsch, M.D.

**APPENDIX****EXPERIMENTAL**

A study was conducted to assess the effect of odorants on the blood flow to the vaginal area of female subjects, a measure of the level of female sexual arousal and excitation. Thirty adult pre-menopausal, periovulatory women volunteered for this IRB approved study.

**SUBJECTS.** Subjects were 18-40 year old females who were not on any prescription or non-prescription medication including oral contraceptives, were literate in English, non-lactating, not actively attempting pregnancy, not smoking for at least one year, consumed less than one drink of alcohol per day, not using cocaine or other illegal drug, and had no genital sexual stimulation by self or their partner for 48 hours prior to the study session.

All subjects scored normosmic on the University of Pennsylvania Smell Identification Test. The subjects had no diseases known to induce autonomic disorders or chemosensory disorders, and were not on medications that produce chemosensory disorders.

**METHOD.** After a female subject was positioned on the examination table, a vaginal process graphic recording device was applied. The device was a sterile monitoring gauge, a photoplethysmograph, similar in shape to a tampon, which was placed into the vagina. The monitoring device measured pulse pressure, which indicates change in blood flow to the vagina. The gauge was hooked up to a computer and changes in pulse strength were recorded on a continual basis.

A three (3) minute period was allowed for acclimation to the experimental environment or a longer duration was allowed until stable baseline measurements were obtained (which measures vaginal bloodflow). A surgical mask untreated with an added odor, was applied over the subject's mouth and nose for one (1) minute. During this time, blood flow to the vagina was recorded.

After the one-minute measurement was taken, the women were asked if the odor was familiar, if they could identify it, and if they liked it or disliked it. Following this, the mask was removed for a three (3) minute no odor "washout" period during which blood flow was measured when no mask was in place. This was to eliminate the effect of the odor - positive or negative - so that blood flow returned to baseline.

In a double-blind, randomized fashion in which neither the subjects nor the test administrators knew which scents were being tested at any given time during the study, ten (10) surgical masks that had been pre-impregnated with different individual odors or odor mixtures were applied in a similar fashion as in the initial blank mask and recorded to obtain in a similar

fashion to the original blank mask. After this, another blank mask and recordings were obtained, with the initial and final blank mask used as markers of baseline.

Bloodflow was determined with the farral vaginal photoplethysmograph, and computer-assisted therapy device as per published protocol. All odors were FDA/GRAS approved and impregnated on molded paper 3M surgical masks at suprathreshold, non-trigeminal levels as determined by an independent panel of the Smell and Taste Treatment Research Foundation.

**Statistical analysis.** Statistical analysis was performed independently by the University of Illinois, School of Public Health. Statistical significance was defined by a "p" value less than or equal to 0.05. Data was statistically analyzed using 5 non-parametric tests of Signed Rank Test, Wilcoxon Rank Sum Test, and Spearman's Rank Correlation Coefficient. (T. Colton, *Statistics in Medicine*, Little Brown & Co., Boston, MA (1974); E.L. Lehmann, *Nonparametrics: Statistical Methods Based on Ranks*, Holden-Day, New York, NY (1975)).

**Olfactory ability tests.** Each female subject was also given a series of tests of olfactory ability.

Subjects underwent standardized olfactory testing with the University of Pennsylvania Smell Identification Tests (UPSiT), a 40-question forced choice scratch-and-sniff test in which the person is given four choices for each question and that has been normalized at age and sex. For example, in one question, an odor is presented, and the individual is asked if the odor is pizza, motor oil, peanuts, or lilac.

Each subject was also given an odor threshold test, the Pyridine Olfactory Threshold test, a forced-choice test during which bottles containing various concentrations of pyridine, a chemical whose odor resembles scallops. This test evaluates the concentration of the odor that must be present before it is detectable.

With this group of tests, olfactory acuity could be established, and those subjects who had a normal sense of smell and those with lesser or no ability to smell.

**Questionnaires.** Subjects also underwent a series of questionnaires regarding demographic data, sexual history data, sexual history and olfactory preference. These included a vaginal bloodflow study questionnaire which queried regarding use of cologne and food hedonics, as well as sexual conduct and behavior. Subjects were questioned as to favorite colognes and whether they or their sexual partner wore a perfume or cologne on a regular basis, favorite and least favorite food, number of sexual partners and encounters in the previous thirty days, sexual preference, and odors that recalled childhood.

The subjects were also questioned about orgasmic functioning, including frequency in the last thirty days and over the previous six months. Through these questions, the number of women who experienced orgasm but did so infrequently, and a group who were multiorgasmic were determined.

**Sexual Arousal Ability Inventory.** The subjects also completed the Sexual Arousal Ability Inventory, a standardized test of assessing ease of arousability on a negative 1 to 5 scale (Hoop, E.F., Hoon, P.W., and Wincze, J.P., The SAL "An Inventory for the Measurement of Female Sexual Arousalability," *Arch. Sex. Behav.* 5:291-300 (1976)), and the Sexual Arousal Ability Inventory which accesses a negative 1 to 5 scale degree of anxiety induced by a variety of sexual activity (Chambles, D.L., and J.L. Lifshitz, "Self-reported Sexual Anxiety and Arousal: The Expanded Sexual Arousalability Inventory," *J. Sex. Research* 20:241-254 (1984)).

Each activity was rated for its ability to arouse or to inhibit arousal. Participants were asked if particular activities were either very arousing (5) or adversely affected their arousal (-1). The twenty eight questions used to assess sexual behaviors were used to rate sexual anxiety. The participants were asked to rate not only what aroused them (or turned them off) but also what activities would induce feelings of anxiety -- defined as extreme uneasiness or distress. The scale was reversed, meaning the -1 indicated that the activity was relaxing or calming and indicated that the activity was extremely anxiety-producing. For example, circling the number 2 in response to a question meant that the activity sometimes caused anxiety or was slightly anxiety-producing. The range allowed for differences not only among individual women, but for each woman, depending on the setting.

**RESULTS.** The effect of odor on blood flow to the vagina was calculated based on changes from the average of the bloodflow measured while the subject was wearing the blank masks. Blood flow to the vagina changes are shown in **Tables I-V**, below.

The sources of odorants in the Tables were as follows:

- Baby powder = International Flavors and Fragrances, Inc. (IFF) (#3169-HS)
- Banana nut bread = Aromatech (#256454)
- Charcoal barbecue smoke = IFF (#2185-HS)
- Cherry = Orchidia (# F180075)
- Chocolate = Florasynth, Inc. (#A3898)
- Cologne = Old Spice®
- Cucumber = Aromatech (#256452)
- Good N' Plenty® (licorice-based) = Aromatech (#236923)
- Lavender = Energy Essentials
- Perfume = Chanel No. 5

Pumpkin pie = Florasynth, Inc. Energy Essentials (#AG-6956)

**Table I** shows the average change in blood flow to the vagina of the entire group of female test subjects (n=30) when administered individual odorants and odorant mixtures.

**TABLE I**  
**AVERAGE % CHANGE IN BLOOD FLOW TO THE VAGINA**  
**IN TOTAL GROUP OF FEMALES**

| ODORANT                                     | % CHANGE IN BLOOD FLOW TO THE VAGINA<br>(OVER BASELINE MEASUREMENT) |
|---|---|
| Licorice-based (Good N' Plenty®) + cucumber | + 13 %  |
| Baby powder                                 | + 13 %  |
| Pumpkin pie + lavender                      | + 11 %  |
| Baby powder + chocolate                     | + 4 %   |
| Perfume                                     | + 0-1 %   |
| Cologne                                     | -1 %  |
| Licorice-based (Good N' Plenty®)            | -12 %   |
| Charcoal barbecue smoke                     | -14 %   |
| Cherry                                      | -18 %   |

As a group, several odorants impaired arousal. Those odors that had the greatest negative effect, meaning that the baseline blood flow measurement actually decreased, were cherry (18-percent reduction) and charcoal barbecue smoke (14-percent reduction).

Other odorants had a lesser effect. Male colognes decreased flow of blood to the vagina by 1 percent, and female perfumes increased it by 1 percent. A combination of baby powder and chocolate resulted in a 4-percent increase.

Pumpkin pie and lavender odorants increased blood flow to the vagina by 11 percent. The odorant that had the greatest effect to induce female sexual arousal was a combination licorice-based odorant and cucumber, which increased blood flow by 13 percent.

**Subgrouping according to masturbation arousal.** While the licorice-based odorant and cucumber combination was arousing to most women, difference occurred among the participants based on the kinds of sexual behavior and activities preferred. It was thus found

that the women could be subgrouped into those who found masturbation arousing and those who did not.

**Table II** shows the average change in blood flow to the vagina of the subgroup of female individuals who indicated a high sexual arousal with masturbation on the questionnaire.

**TABLE II**  
**FEMALES WITH HIGH AROUSAL WITH MASTURBATION**

| ODORANT   | % CHANGE IN BLOOD FLOW TO THE<br>VAGINA<br>(OVER BASELINE MEASUREMENT) |
|---|--|
| Licorice-based (Good N' Plenty®) + banana nut bread | + 28 %   |
| Licorice-based (Good N' Plenty®) + cucumber         | + 22 %   |
| Perfume   | + 18 %   |

**Table III** shows the average change in blood flow to the vagina of the subgroup of female individuals who indicated repulsion or low arousal with masturbation on the questionnaire.

**TABLE III**  
**FEMALES WITH INHIBITION OR LOW AROUSAL WITH MASTURBATION**

| ODORANT                          | % CHANGE IN BLOOD FLOW TO THE<br>VAGINA<br>(OVER BASELINE MEASUREMENT) |
|----------------------------------|--|
| Baby powder                      | + 16 %   |
| Pumpkin pie + lavender           | + 10 %   |
| Licorice-based (Good N' Plenty®) | -20 %  |

Among women who reported being extremely aroused by masturbation, every odor tested had an arousing effect. A licorice-based odorant and banana-nut bread combination (28-percent increase) and the licorice-based odorant and cucumber combination (22 percent) showed the

greatest effect. Popular perfumes showed an 18-percent increase in blood flow to the vagina, as did baby powder, which was nearly as arousing at a 16-percent increase.

Women who did not find masturbation extremely arousing showed an increase in blood flow to the vagina of 16 percent in response to baby powder and a 1-percent response to lavender and pumpkin pie.

**Subgrouping according to arousal by manual genital stimulation.** The women could also be subgrouped into those who were extremely aroused when a lover manually stimulated her genitals and those who were not.

**Table IV** shows the average percent change in blood flow to the vagina of the subgroup of female individuals who indicated that they are positively aroused sexually by partner's finger manipulation of the genitals on the questionnaire.

**TABLE IV**  
**FEMALES WHO ARE POSITIVELY AROUSED**  
**BY GENITAL FINGER MANIPULATION BY PARTNER**

| ODORANT                                     | % CHANGE IN BLOOD FLOW TO THE<br>VAGINA (OVER BASELINE<br>MEASUREMENT) |
|---|--|
| Licorice-based (Good N' Plenty®) + cucumber | + 18 %   |
| Pumpkin pie + lavender                      | + 12 %   |

**Table V**, below, shows the average percent change in blood flow to the vagina of the subgroup of female individuals who indicated a low to zero to negative level of arousal by partner's finger manipulation of the genitals on the questionnaire.

**TABLE V**  
**FEMALES WHO ARE NEGATIVELY AROUSED**  
**BY GENITAL FINGER MANIPULATION BY PARTNER**

| ODORANT  | % CHANGE IN BLOOD FLOW TO THE<br>VAGINA (OVER BASELINE<br>MEASUREMENT) |
|--|--|
| Perfume  | - 14 %   |
| Pumpkin pie + lavender                                   | - 12 %   |
| Licorice-based (Good N' Plenty <sup>®</sup> ) + cucumber | - 13 %   |

Women who found manual genital stimulation arousing showed a 12-percent increase in blood flow to the vagina in response to pumpkin pie and lavender, and averaged an 18-percent increase with the licorice-based odorant and cucumber combination.

No odors induced sexual arousal in the women who were not extremely aroused by manual genital stimulation, whereas many odors inhibited arousal, including male colognes and perfumes, both of which decreased blood flow by 14 percent. The licorice-based odorant and cucumber combination decreased blood flow by 13 percent in that group.